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GRNO-04U1

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EXAMINER

KUBELIK, ANNE R

ART UNIT

PAPER NUMBER

1638

MAIL DATE

DELIVERY MODE

09/24/2009

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

|                              |                                      |                                    |  |
|------------------------------|--------------------------------------|------------------------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b><br>10/089,450 | <b>Applicant(s)</b><br>GORR ET AL. |  |
|                              | <b>Examiner</b><br>Anne R. Kubelik   | <b>Art Unit</b><br>1638            |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 29 June 2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-3, 17 and 22-24 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3, 17 and 22-24 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 29 June 2009 has been entered.

2. Claims 1-3, 17 and 22-24 are pending.

3. The rejection of claims 1-3 and 17 under 35 U.S.C. 103(a) as being unpatentable over Reutter et al (1996, Plant Tiss. Cult. Biotechnol. 2:142-147) in view of Lee et al (US Patent 6,020,169, filed April 1998) is withdrawn in light of the Declaration of Gunthur Neuhaus.

4. The rejection of claims 1-3 and 17 under 35 U.S.C. 103(a) as being unpatentable over Reutter et al in view of Lee et al further in view of Nasu et al (1997, J. Ferm. Bioengin. 84:519-523) is withdrawn in light of the Declaration of Gunthur Neuhaus.

### ***Claim Rejections - 35 USC § 112***

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 23 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

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Neither the instant specification nor the originally filed claims appear to provide support for the expression of F(ab) or F(ab')<sub>2</sub> in protonema. The specification, on pg 6, to which Applicant pointed to for support in the amendment filed 7 June 2009, only provides support for expression of antibodies or functional fragments thereof, not support for the specific functional fragments F(ab) or F(ab')<sub>2</sub>.

Thus, such a concept constitutes NEW MATTER. In response to this rejection, Applicant is required to point to support for the concept] or to cancel the new matter.

7. Claims 1-3, 17 and 22-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolating a heterologous protein from culture medium in which in transformed *Physcomitrella patens* protonema were grown, wherein the protonema were transformed with a construct encoding a secretion transit peptide operably linked to the heterologous protein, does not reasonably provide enablement for isolating a heterologous protein from culture medium in which in transformed *Physcomitrella patens* protonema were grown, wherein the protonema were transformed with a construct encoding other kinds of transit peptide operably linked to the heterologous protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to isolating a heterologous protein from culture medium in which in transformed *Physcomitrella patens* protonema were grown, wherein the protonema were transformed with a construct encoding any transit peptide operably linked to the heterologous protein.

The instant specification, however, only provides guidance for transformation of *P. patens* With a vector encoding vascular endothelial growth factor (VEGF) operably linked to a human ER transit peptide (pg 14-27).

Transit peptides that direct the protein to the mitochondria or chloroplast would not function in the claimed method, as use of these transit peptides would not result in the secretion of the heterologous protein.

Given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate methods for solating a heterologous protein from culture medium in which in transformed *Physcomitrella patens* protonema were grown, wherein the protonema were transformed with a construct encoding a transit peptide that directs a protein to the mitochondria or chloroplast operably linked to the heterologous protein.

### ***Claim Rejections - 35 USC § 103***

8. Claims 1-3, 17 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reutter et al (1996, Plant Tiss. Cult. Biotechnol. 2:142-147) in view of Raskin et al (US Patent 6,096,546, filed January 1998).

The claims are drawn to a method of isolating a heterologous protein from culture medium in which in transformed *Physcomitrella patens* protonema were grown.

Reutter et al teach growth of *P. patens* protonema transformed with a nucleic acid encoding a heterologous protein in a bioreactor culture (pg 143, paragraph 2-3) and that these protonema produced large amounts of the heterologous protein grown in bioreactor culture (pg

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143, paragraph 3; Fig. 2-3; claim 1). Reutter et al also teach that *P. patens* can be grown on inorganic medium (pg 142, paragraph 4). Reutter et al do not disclose isolation of the protein from the culture medium.

Raskin et al teach isolation of biologically active heterologous protein from the medium in which plants are grown (column 9, lines 21-35; column 10, lines 45-58; column 12, lines 22-67; claims 1-11). The heterologous protein was expressed from a construct containing a signal peptide for secretion (column 6, line 63, to column 7, line 20; Fig. 1 and 4). The heterologous proteins include the enzyme xylanase (example 3).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of producing heterologous protein in *P. patens* protonema as taught by Reutter et al, to use a signal peptide in the transformation construct and isolate the protein from media as described in Raskin et al. One of ordinary skill in the art would have been motivated to do so because of the advantages of being able to isolate the protein from the medium (Raskin et al, column 3, lines 42-67).

In the Reski Declaration filed 13 October 2006, Declarant states that because protonema are not capable of rhizosecretion or secretion through stomata, processes that require root pressure lacking in protonema (Declaration ¶47)

This is not found persuasive because Raskin et al teach that in plants the heterologous proteins are secreted as a result of diffusion, facilitated transport or xylem pressure (column 4, lines 57-67); the first two would apply to protonema. Clearly the plant's cell wall is no barrier to secretion of heterologous proteins. Given the advantages of being able to isolate the protein

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form the medium without having to disrupt plant tissue, it would be obvious to one of skill in the art to try this method with Reutter et al's protonema system.

9. Claims 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reutter et al in view of Raskin et al as applied to claims 1-3, 17 and 24 above, and further in view of Hein et al (US Patent 5,959,177, filed May 1996).

The claims are drawn to a method of isolating antibody or Fab from culture medium in which in transformed *Physcomitrella patens* protonema were grown.

The teachings of Reutter et al in view of Raskin et al are discussed above. Reutter et al in view of Raskin et al do not teach expression of antibodies or FAb fragments in the plants.

Hein et al teach production of antibody in plants (column 46, line 34, to column 49, line 40).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of isolating heterologous protein from culture medium in which in transformed *Physcomitrella patens* protonema were grown taught by Reutter et al in view of Raskin et al to use an antibody, including Fab, as the heterologous protein as described in Hein et al. One of ordinary skill in the art would have been motivated to do so because of the advantages of a system in which large quantities of an economically important heterologous protein can be produced and isolated. It would be obvious to one of skill in the art to express a Fab in the plants, because of the suggestion of Hein et al to do so (column 11, lines 53-56).

### ***Conclusion***

10. No claim is allowed.

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11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, Ph.D., whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached at (571) 272-0975.

The central fax number for official correspondence is (571) 273-8300.

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September 24, 2009

/Anne R Kubelik/

Primary Examiner, Art Unit 1638